

Plasma glycerol concentration in patients with myocardial ischaemia and arrhythmias

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Plasma glycerol concentration was estimated in patients admitted to hospital because of acute chest pain. The patients were later divided into different groups according to their diagnosis, e.g. myocardial infarction with arrhythmias, uncomplicated myocardial infarction, angina, and pains of noncardiac origin. Patients with myocardial infarction complicated by arrhythmias showed significantly higher plasma glycerol concentrations than patients with uncomplicated infarction or angina. Plasma glycerol concentration, which is a better index of lipid mobilization and, indirectly, of the sympathetic activity, than plasma free fatty acid level, might be used to select cases with myocardial infarction prone to get complicating arrhythmias.

Serum concentrations of free fatty-acid (FFA) have been shown to be raised in patients with acute myocardial infarction by Kurien and Oliver (1966). In a more detailed study the same authors (Oliver, Kurien, and Greenwood, 1968) found a positive relation between serum FFA levels and complicating arrhythmias and death after myocardial infarction. They postulated that the rise of serum FFA was a consequence of mobilization of FFA from adipose tissue, induced by noradrenaline. In other studies, the level of catecholamines in the urine was shown to be raised in cases of acute myocardial infarction complicated by arrhythmias and/or cardiogenic shock (Jewitt *et al.*, 1969), and plasma noradrenaline concentration was raised after myocardial infarction and related – directly or indirectly – to the development of serious arrhythmias (McDonald *et al.*, 1969). It follows that both these latter studies support the theory that the rise in the plasma FFA concentration in cases with myocardial infarction could be secondary to catecholamine-induced fatty acid mobilization from adipose tissue.

During the lipolysis of triglycerides in adipose tissue, glycerol is formed in addition to free fatty acids and is released to plasma. In contrast to free fatty acids, glycerol cannot be reused in adipose tissue or muscle (Steinberg, 1964; Havel, 1965) and therefore is a better index of the rate of adipose tissue lipolysis than the plasma FFA.

The present study was started in order to elucidate (1) whether a relation existed between plasma glycerol concentration and complicating arrhythmias during acute myocardial infarction, and (2) whether determination of plasma glycerol concentration could be used for selecting cases with myocardial infarction prone to get complicating arrhythmias. Rutenberg, Pamintuan, and Soloff (1969) found no relation between the initial level of serum FFA and the future development of complications, but, as stated above, the plasma glycerol might be a more discriminative parameter than FFA.

There is some evidence in favour of the theory that the arrhythmias during acute myocardial infarction are due to a direct deleterious effect of free fatty acids on the injured myocardium (Kurien, Yates, and Oliver, 1969; Henderson, Most, and Sonnenblick, 1969; Gupta *et al.*, 1969; Taylor *et al.*, 1969; Kurien and Oliver, 1970), but, as yet, it cannot be excluded that the lipid mobilization and the heart arrhythmias both are direct effects of the rise of the plasma catecholamine level (Nelson, 1970). However, whether this theory is correct or not, the plasma glycerol theoretically could be of value as a predicting index and was therefore judged as worth testing.

Subjects

The material consisted of 184 patients who were admitted to hospital with acute chest pain. Patients with diabetes mellitus and patients given theophyllamine and/or sympathomimetic drugs were excluded. None of the patients showed any

clinical signs of failure or shock when the samples were taken.

The study was divided into two separate series.

In *series A* capillary blood was used and the samples had to be taken at fixed times during the day, e.g. at 9 a.m., noon, and 3 p.m. The patients in both the series were looked after under the same conditions in the coronary care unit of the hospital.

In *series B* the venous blood samples were taken immediately on admission to hospital.

In *series A* the first blood samples were taken 2–18 hours after the onset of symptoms whereas blood samples in *series B* were taken 2–7 hours after onset. The mean time elapsed between onset of symptoms and taking of samples was about the same in the different groups in respective series.

Diagnostic criteria The diagnosis of myocardial infarction was based on electrocardiographic evidence, using the criteria recommended by WHO, and significantly raised serum levels of aspartate aminotransferase (SGOT). Arrhythmias were displayed on bedside oscilloscopes with intermittent direct recordings. Arrhythmias were considered to be present if there were more than 6 ventricular extrasystoles a minute or more serious disturbances of heart rhythm (atrial flutter or fibrillation, ventricular fibrillation).

In *series A* patients were divided retrospectively into four different groups according to their diagnosis (Table 1). These groups and the age and sex of the patients are shown in Table 1.

Patients with previous infarctions and/or previous histories of angina were classified in group II. In these patients the suspicion of myocardial infarction could not be verified with electrocardiograms or SGOT levels. Group I consisted of subjects with chest pain of non cardiac origin.

In *series B*, the same classification was used, except that the patients with previous infarction and/or angina were separated into two groups (II and III), depending on the absence or the presence of arrhythmias. Thus, the patients in *series B* were divided into five groups. Details of these patients are summarized in Table 2.

Methods

The determination of plasma FFA was made according to Laurell and Tibbling (1967). Plasma glycerol concentration was determined according to the method described by the same authors (Laurell and Tibbling, 1966). The statistical evaluation was made using Wilcoxon's rank sum test (Wilcoxon, 1945).

Results

Plasma FFA and glycerol values of the four groups of patients in *series A* are shown in Fig. 1 and 2. The mean glycerol value of the patients in group IV was significantly higher than those of groups II and III (Table 3). No significant differences between the mean FFA values of the groups were found.

TABLE 1 Number, age, and sex of patients in different groups in series A

Group	Diagnosis	Men			Women			Total		
		No.	Age (yr) Mean	Range	No.	Age (yr) Mean	Range	No.	Age (yr) Mean	Range
I	Chest pains, non cardiac	4	54.8	37–67	3	67.3	48–77	7	60.1	37–77
II	Angina	16	67.3	58–82	3	73.0	67–78	19	68.2	58–82
III	Myocardial infarction	15	60.4	40–83	3	65.7	63–68	18	61.3	40–83
IV	Myocardial infarction complicated by arrhythmias	15	64.0	42–86	6	74.0	63–84	21	66.9	42–86

TABLE 2 Number, age, and sex of patients in different groups in series B

Group	Diagnosis	Men			Women			Total		
		No.	Age (yr) Mean	Range	No.	Age (yr) Mean	Range	No.	Age (yr) Mean	Range
I	Chest pains, non cardiac	7	67.1	48–86	6	60.2	21–80	13	63.9	21–86
II	Angina, no arrhythmias	29	66.1	49–89	8	71.5	59–83	37	67.3	49–89
III	Angina complicated by arrhythmias	10	71.8	55–88	8	72.8	54–89	18	72.2	54–89
IV	Myocardial infarction, no arrhythmias	22	66.0	50–83	9	75.2	68–89	31	68.6	50–89
V	Myocardial infarction complicated by arrhythmias	16	68.0	42–87	4	69.3	54–85	20	68.3	42–87

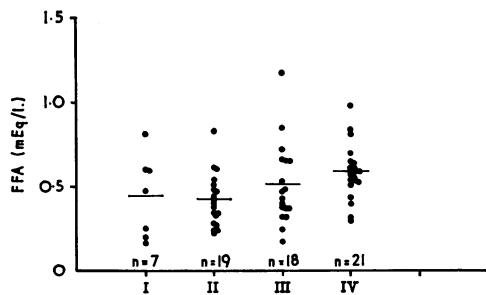


FIG. 1 The individual mean plasma FFA concentrations during the first day in hospital of the patients in the four groups in series A. For explanation of the diagnostic groups I-IV see Table 1. The mean concentrations of the groups are indicated by horizontal lines.

Plasma FFA and glycerol values of the five groups from series B are shown in Fig. 3 and 4. No significant differences were noticed when comparing the mean FFA values of the groups, but the mean glycerol value of group V was significantly raised in comparison with those of groups I and II. Also the mean

FIG. 2 The individual mean plasma glycerol concentrations during the first day in hospital of the four groups in series A. For an explanation of the diagnostic groups I-IV see Table 1. The mean concentrations of the groups are indicated by horizontal lines.

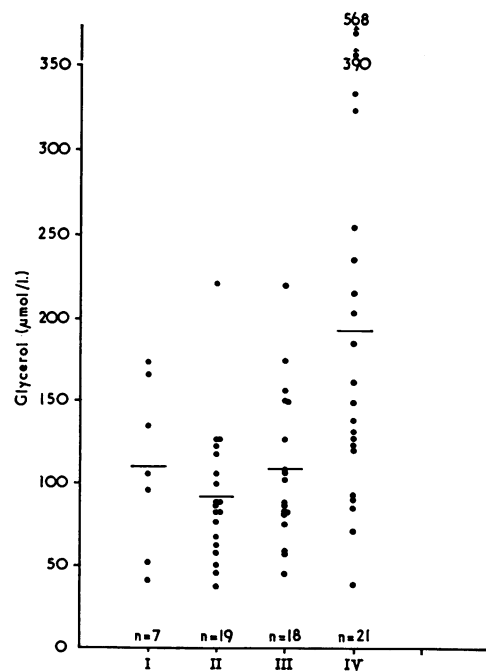


TABLE 3 Significance levels (*P* values) in comparison between groups in series A, using mean capillary glycerol concentration during first day in hospital. Wilcoxon's rank sum test was used

Group	I	II	III	IV
I	—	NS	NS	NS
II	NS	—	NS	<0.01
III	NS	NS	—	<0.02
IV	NS	<0.01	<0.02	—

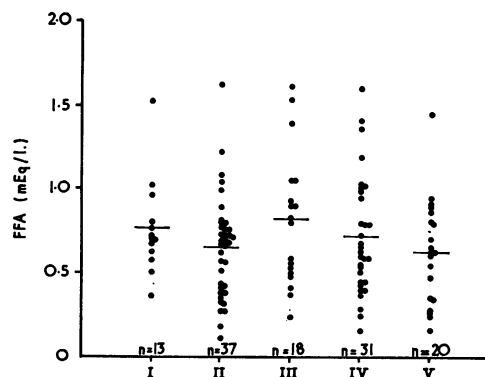
NS = not significant.

glycerol value of group III was significantly raised in comparison with that of group II. The differences between the groups are summarized in Table 4.

In Fig. 5 plasma FFA values of all the patients in series B are plotted against plasma glycerol values. There was a highly significant correlation between plasma FFA and glycerol concentrations ($P < 0.001$), but the glycerol concentration was clearly the more sensitive parameter of the two. Similar results were obtained when plotting plasma FFA/glycerol data from series A.

Some of the patients with myocardial infarction complicated by arrhythmias died during their stay in hospital, but their glycerol levels did not differ significantly from the other patients' in their respective groups. Any differences between the men and women were not found in any of the groups as regards plasma FFA and glycerol.

FIG. 3 The individual plasma FFA concentrations of the patients in the 5 groups in series B. For an explanation of the diagnostic groups I-V, see Table 2. The mean concentration of the groups is indicated by horizontal lines.



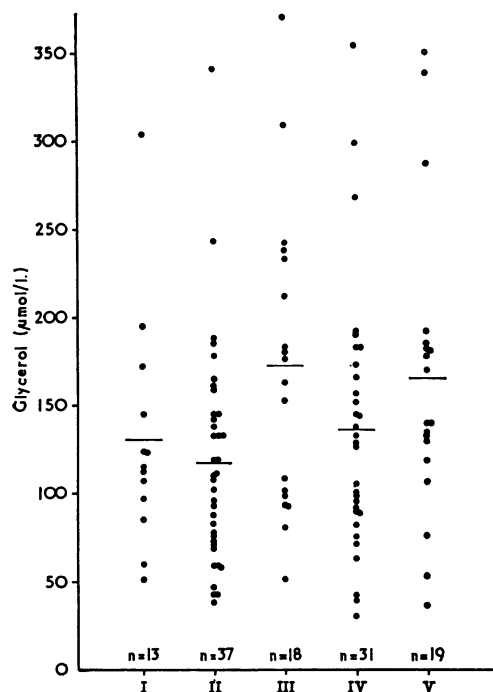


FIG. 4 The individual plasma glycerol concentrations of the patients in the five groups in series B. For explanation of the diagnostic groups I-V, see Table 2. The mean concentrations of the groups are indicated by horizontal lines.

Discussion

For reasons given in the introduction, plasma glycerol concentration is considered a better measure of the rate of lipid mobilization and, indirectly, of sympathetic activity than plasma FFA concentration. Furthermore, plasma glycerol concentration is the more sensitive index of both.

In both series, patients with myocardial infarction complicated by arrhythmias were

TABLE 4 Significance levels (*P* values) in comparison between groups in series B, using venous plasma glycerol value on admission. Wilcoxon's rank sum test was used.

Group	I	II	III	IV	V
I	—	NS	NS	NS	<0.05
II	NS	—	<0.02	NS	<0.05
III	NS	<0.02	—	NS	NS
IV	NS	NS	NS	—	NS
V	<0.05	<0.05	NS	NS	—

NS = not significant.

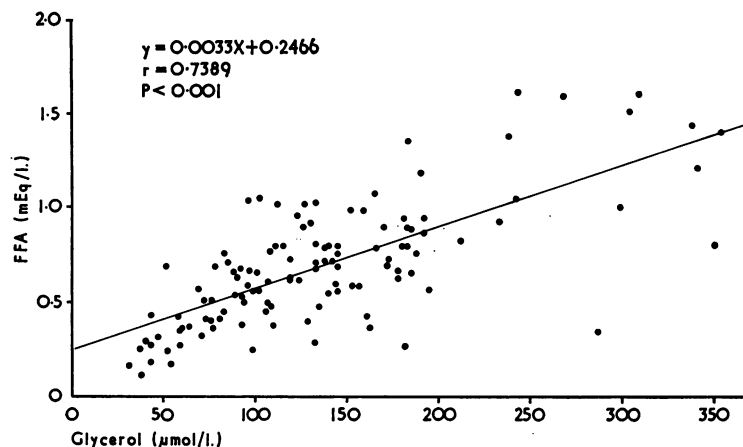


FIG. 5 The individual plasma FFA concentrations of the patients in series B plotted against their plasma glycerol concentrations. Above, in the figure the equation of the regression line, the correlation coefficient, and the *P* value of the correlation are shown.

found to have higher levels of plasma glycerol than patients with angina and those with myocardial infarction without arrhythmias. In addition, patients in series B with angina complicated by arrhythmias showed an increase of plasma glycerol concentration in comparison with patients with uncomplicated angina. Thus, the main correlation was between plasma glycerol increase and complicating arrhythmias, and it was of minor influence whether a myocardial infarction was present or not. Thus, the plasma glycerol concentration may be of value as a means of predicting arrhythmias.

In series A, the mean capillary glycerol concentration during the first day in hospital was used. For practical reasons, the samples were taken at fixed hours, which is a drawback, because the samples ought to be taken immediately on admission to the hospital. In series B, the samples were taken at once on admission, but venous blood was used and the venous glycerol concentration is known to vary more than that of the arterial (Gordon and Cherkes, 1956) and capillary blood. Of course, capillary samples taken immediately on admission would be preferable, and such a study has now been initiated.

In our opinion, the present results merit further investigations.

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References

- Gordon, R. S., and Cherkes, A. (1956). Unesterified fatty acid in human blood plasma. *Journal of Clinical Investigation*, **35**, 206.
- Gupta, D. K., Young, R., Jewitt, D. E., Hartog, M., and Opie, L. H. (1969). Increased plasma-free-fatty-acid concentrations and their significance in patients with acute myocardial infarction. *Lancet*, **2**, 1209.
- Havel, R. J. (1965). Some influences of the sympathetic nervous system and insulin on mobilization of fat from adipose tissue: Studies of the turnover rates of free fatty acids and glycerol. *Annals of the New York Academy of Sciences*, **131**, 91.
- Henderson, A. H., Most, A. S., and Sonnenblick, E. H. (1969). Depression of contractility in rat heart muscle by free fatty acids during hypoxia. *Lancet*, **2**, 825.
- Jewitt, D. E., Mercer, C. J., Reid, D., Valori, C., Thomas, M., and Shillingford, J. P. (1969). Free noradrenaline and adrenaline excretion in relation to the development of cardiac arrhythmias and heart-failure in patients with acute myocardial infarction. *Lancet*, **1**, 635.
- Kurien, V. A., and Oliver, M. F. (1966). Serum-free-fatty-acids after acute myocardial infarction and cerebral vascular occlusion. *Lancet*, **2**, 122.
- Kurien, V. A., and Oliver, M. F. (1970). Arrhythmogenic action of free fatty acids in myocardial hypoxia. Abstracts VI World Congress of Cardiology, London, p. 240.
- Kurien, V. A., Yates, P. A., and Oliver, M. F. (1969). Free fatty acids, heparin, and arrhythmias during experimental myocardial infarction. *Lancet*, **2**, 185.
- Laurell, S., and Tibbling, G. (1966). An enzymatic fluorometric micromethod for the determination of glycerol. *Clinica Chimica Acta*, **13**, 317.
- Laurell, S., and Tibbling, G. (1967). Calorimetric micro-determination of free fatty acids in plasma. *Clinica Chimica Acta*, **16**, 57.
- McDonald, L., Baker, C., Bray, C., McDonald, A., and Restieaux, N. (1969). Plasma-catecholamines after myocardial infarction. *Lancet*, **2**, 1021.
- Nelson, P. G. (1970). Free fatty acids and cardiac arrhythmias. *Lancet*, **1**, 783.
- Oliver, M. F., Kurien, V. A., and Greenwood, T. W. (1968). Relation between serum-free-fatty-acids and arrhythmias and death after acute myocardial infarction. *Lancet*, **1**, 710.
- Rutenberg, H. L., Pamintuan, J. C., and Soloff, L. A. (1969). Serum-free-fatty-acids and their relation to complications after acute myocardial infarction. *Lancet*, **2**, 559.
- Steinberg, D. (1964). Synthesis and breakdown of triglycerides in adipose tissue. In *Fat as a Tissue*, p. 127. Ed. by K. Rodahl and B. Issekutz. McGraw-Hill, New York.
- Taylor, S. H., Saxton, C., Majid, P. A., Dykes, J. R. W., Ghosh, P., and Stoker, J. B. (1969). Insulin secretion following myocardial infarction with particular respect to the pathogenesis of cardiogenic shock. *Lancet*, **2**, 1373.
- Wilcoxon, F. (1945). Individual comparisons by ranking methods. *Biometrics*, **1**, 80.